PTO 1542
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U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

## ONLINE SEARCH REQUEST FORM

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USER Toni Scheiner SERIAL NUMBER 08/083596

ART UNIT 1806 PHONE 308-3963 DATE 7/24/96

Please give a detailed statement of requirements. Describe as specifically as possible the subject matter to be searched. Define any terms that may have special meaning. Give examples or relevant citations, authors, or keywords, if known.

You may include a copy of the broadest and or relevant claim(s).

please do an interference search for Seq ID NOS. 5 thru 11

Thanks,

Toni

?t s9/7/1-16

9/7/1 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI
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009855324 WPI Acc No: 94-135180/16
XRAM Acc No: C94-062475
XRPX Acc No: N94-106287
Notch protein and nuclear acid compositions - is used for treatment of disorders of cell fate or differentiation esp. breast, colon or cervical cancer
Patent Assignee: (UYYA ) UNIV YALE
Author (Inventor): ARTAVANIS-TSAKONAS S; BLAUMUELLER C M; FEHON R G; ZAGOURAS P
Number of Patents: 002
Number of Countries: 045
Patent Family:

| CC | Number | Kind | Date | Week | |
|---|---|---|---|---|---|
| WO | 9407474 | A1 | 940414 | 9416 | (Basic) |
| AU | 9453503 | A | 940426 | 9432 | |

Priority Data (CC No Date): US 955012 (920930); US 83590 (930625)
Applications (CC,No,Date): AU 9453503 (930930); WO 93US9338 (930930)
Language: English
EP and/or WO Cited Patents: 6.Jnl.Ref; US 5115096; US 5132212; US 5264557
Designated States
(National): AU; BB; BG; BR; BY; CA; CZ; FI; HU; JP; KP; KZ; LK; LV; MG; MN; MW; NO; NZ; PL; RO; RU; SD; SK; UA; US; UZ; VN
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; OA; PT; SE
Filing Details: AU9453503 Based on WO 9407474
Abstract (Basic): WO 9407474 A
The pharmaceutical compsn. comprises a therapeutically effective amt. of a Notch protein (A) and a pharmaceutically acceptable carrier.
USE - The comosns. can be used for treatment of disorders of cell fats or differentiation. The therapeutic compsns. include Notch proteins and analogues, derivs. and fragments, antibodies, nucleic acid encoding, analogues and derivs., Notch antisense nucleic acids, tooorythmic proteins and derivs. which bind or interact with Notch proteins, their encoding nucleic acids or Abs. The compsn. is pref. admin. to a cancerous condition, e.g. breast, colon or cervical cancer, or to prevent progression from a pre-neoplastic or non-malignant state into a neoplastic or malignant state. Dwg.0/17
Derwent Class: B04; D16; S03;
Int Pat Class: A61K-031/70; A61K-037/02; A61K-039/395; A61K-039/44; C07H-021/04; G01N-033/53; G01N-033/68

9/7/2 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
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164909 DBA Accession No.: 94-07460 PATENT

Notch protein and antisense DNA - application in carcinoma diagnosis, therapy and gene therapy
PATENT ASSIGNEE: Univ.Yale 1994
PATENT NUMBER: WO 9407474 PATENT DATE: 940414 WPI ACCESSION NO.: 94-135180 (9416)
PRIORITY APPLIC. NO.: US 83590 APPLIC. DATE: 930625
NATIONAL APPLIC. NO.: WO 93US9338 APPLIC. DATE: 930930
LANGUAGE: English
ABSTRACT: A pharmaceutical composition comprising a Notch protein (A) and a carrier is claimed. More specifically, the composition comprises a human Notch protein encoded by a specified DNA sequence which is bound by an antibody to a Notch protein. The following are also claimed: (1) a pure human Notch protein homolog of specified protein sequence; (2) nucleic acid encoding the protein of (1); (3) a recombinant cell containing the nucleic acid of (2); (4) a composition comprising a Notch protein or derivative (e.g. chimeric protein); (5) a composition comprising a molecule which antagonizes the function of a Notch protein; and (6) the use of the composition of (5) for treatment of cervix carcinoma, mamma carcinoma or colon carcinoma. In (4), the chimeric protein may include functionally active portions of the Notch protein encoded by human cDNA contained in plasmid phN3k (ATCC 68609) and plasmid phN5k (ATCC 68611). The therapeutic composition includes Notch proteins and analogs, antibodies, nucleic acid encoding the analogs, antisense nucleic acids, etc. which bind and interact with Notch proteins, their encoding nucleic acids or antibodies. (232pp)

9/7/3 (Item 1 from file: 399)
DIALOG(R)File 399:CA Search(R)
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121026887 CA: 121(3)26887m PATENT
Therapeutic and diagnostic methods and compositions based on Notch proteins and nucleic acids
INVENTOR(AUTHOR): Artavanis-Tsakonas, Spyridon; Fehon, Richard Grant; Zagouras, Panayiotis; Blaumueller, Christine Marie
LOCATION: USA
ASSIGNEE: Yale University
PATENT: PCT International ; WO 9407474 A1 DATE: 940414
APPLICATION: WO 93US9338 (930930) *US 955012 (920930) *US 83590 (930625)
PAGES: 232 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-031/00A; A61K-031/70B; A61K-037/02B; A61K-039/44B; A61K-039/395B; C07H-021/04B; G01N-033/53B; G01N-033/68B DESIGNATED COUNTRIES: AU; BB; BG; BR; BY; CA; CZ; FI; HU; JP; KR; KZ; LK; LV; MG; MN; MW; NO; NZ; PL; RO; RU; SD; SK; UA; US; UZ; VN DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT ; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA201006 Pharmacology
CA209XXX Biochemical Methods
IDENTIFIERS: human Notch protein therapeutic, cDNA antibody human Notch
DESCRIPTORS:
Gene,animal...
cDNA, for human Notch protein and Drosophila Delta protein
Deoxyribonucleic acid sequences,complementary...
for human Notch protein and Drosophila Delta protein

Alopecia... Cirrhosis... Intestine,neoplasm, colon, inhibitors... Keloid...
Lung,neoplasm, inhibitors... Mammary gland,neoplasm, inhibitors... Neoplasm
inhibitors,colon... Neoplasm inhibitors,lung... Neoplasm inhibitors,mammary
gland... Neoplasm inhibitors,melanoma... Psoriasis...
    Notch protein as diagnosistics and
Proteins,specific or class, gene Delta...
    Notch protein as therapeutics in relation to
Deoxyribonucleic acids,complementary, antisense...
    of human Notch gene, for diagnostics and therapeutics
Protein sequences...
    of human Notch protein and Drosophila Delta protein
Gene,animal, Serrate...
    protein of, Notch protein as therapeutics in relation to
Antibodies... Antibodies,monoclonal...
    to human Notch protein, for diagnostics and therapeutics
Testis,neoplasm, seminoma... Uterus,neoplasm, cervix...
    treatment and diagnosis of, Notch protein as diagnosistics and
  CAS REGISTRY NUMBERS:
146636-21-7  amino acid sequence of
156067-46-8  156067-47-9  156067-48-0  156067-49-1  156067-50-4
    156067-51-5  amino acid sequence of, therapeutics contg.
146636-19-3  human Notch protein homologous to, as therapeutics
148513-28-4  156067-52-6  156067-53-7  156067-54-8  156067-55-9  nucleotide
    sequence of
146636-08-0  146636-13-7  156067-43-5  156067-44-6  156067-45-7  nucleotide
    sequence of, therapeutics contg. protein encoded by

 9/7/4     (Item 1 from file: 434)
DIALOG(R)File 434:SciSearch(R)
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12982219  Genuine Article#: NF965  Number of References: 29
Title: EP-CAM - A HUMAN EPITHELIAL ANTIGEN IS A HOMOPHILIC CELL-CELL
    ADHESION MOLECULE
Author(s): LITVINOV SV; VELDERS MP; BAKKER HAM; FLEUREN GJ; WARNAAR SO
Corporate Source: LEIDEN UNIV,DEPT PATHOL,WASSENAARSEWEG 62,POB 9603/2300
    RC LEIDEN//NETHERLANDS/
Journal: JOURNAL OF CELL BIOLOGY, 1994, V125, N2 (APR), P437-446
ISSN: 0021-9525
Language: ENGLISH  Document Type: ARTICLE
Abstract: The epithelial glycoprotein 40 (EGP40, also known as GA733-2,
    ESA, KSA, and the 17-1A antigen), encoded by the GA-733-2 gene, is
    expressed on the baso-lateral cell surface in most human simple
    epithelia. The protein is also expressed in the vast majority of
    carcinomas and has attracted attention as a tumor marker. The function
    of the protein is unknown. We demonstrate here that EGP40 is an
    epithelium-specific intercellular adhesion molecule. The molecule
    mediates, in a Ca2+-independent manner, a homophilic cell-cell adhesion
    of murine cells transfected with the complete EGP40 cDNA. Two murine
    cell lines were tested for the effects of EGP40 expression:
    fibroblastic L cells and dedifferentiated mammary carcinoma L153S
    cells. The expression of the EGP40 protein causes morphological changes
    in cultures of transfected cells-increasing intercellular adhesion of
    the transfectants-and has a clear effect on cell aggregating behavior
    in suspension aggregation assays. EGP40 directs sorting in mixed cell

populations, in particular, causes segregation of the transfectants from the corresponding parental cells. EGP40 expression suppresses invasive colony growth of L cells in EHS-matrigel providing tight adhesions between cells in growing colonies. EGP40 can thus be considered a new member of the intercellular adhesion molecules. In its biological behavior EGP40 resembles to some extent the molecules of the immunoglobulin superfamily of cell adhesion molecules (CAMs), although no immunoglobulin-like repeats are present in the EGP40 molecule. Certain structural similarities in general organization of the molecule exist between EGP40 and the lin-12/Notch proteins. A possible role of this adhesion molecule in formation of architecture of epithelial tissues is discussed. To reflect the function of the molecule the name Ep-CAM for EGP40 seems appropriate.

9/7/5 (Item 1 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00085740
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Idiopathic, Progressive Mononeuropathy in Young People (ARTICLE)

ENGSTROM, JOHN W.; LAYZER, ROBERT B.; OLNEY, RICHARD K.; EDWARDS, MICHAEL B.
Archives of Neurology
January, 1993; Original: p20
LINE COUNT: 00252
0003-9942

We describe six young patients with insidiously progressive, painlessweakness in the distribution of a single major lower extremity nerve.No cause could be found despite extensive evaluation, including surgical exploration. At the time of diagnosis, all patients had weakness and three patients had sensory loss. In all cases, electromyography revealed a chronic axonal mononeuropathy without conduction block or focal conduction slowing. Magnetic resonance, computed tomographic, and ultrasound imaging studies did not identifya region of nerve swelling, mass, or compression. At surgical exploration, the nerve appeared atrophic in two patients, indurated in one patient, and normal in two patients. Biopsy specimens obtainedfrom two abnormal nerves revealed either wallerian degeneration or endoneurial fibrosis. The clinical features of these patients comprise an unusual clinical entity with no known cause or treatment. (Arch Neurol. 1993;50:)

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

9/7/6 (Item 2 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00052771

Mandibular Reconstruction With a Recombinant Bone-Inducing Factor: Functional, Histologic, and Biomechanical Evaluation (Article)

Toriumi, Dean M., MD; Kotler, Howard S., MD; Luxenberg; Deborah P.; Holtrop, Marijke E., MD, PhD; Wang, Elizabeth A., PhD
Archives of Otolaryngology-Head & Neck Surgery
1991; 117: 1101 (12)
0003-9977

Bone morphogenetic protein-2 (BMP-2) is a human recombinant bone-inducing factor that stimulates bone formation within 14 days. Twenty-six dogs underwent reconstruction of 3-cm full-thickness mandibular defects. After stabilizing the defects with stainless steel reconstruction plates, test implants composed of inactive dog bone matrix carrier and human recombinant BMP-2 were placed in defects of 12 animals (group 1). Control implants (carrier without BMP-2) were used in 10 animals (group 2), and no implants were placed in mandibular defects of four animals (group 3). Animals were killed at 3 and 6 months. The reconstructed segments were evaluated by roentgenography, analysis of functional stability, histology, histomorphometry, and analysis of biomechanical strength using three-point bend testing. In group 1, reconstruction plates were removed at 10 weeks because stiff, noncompressible mineralized bone formed across the defects, allowing the animals to chew a solid diet. The defects from groups 2 and 3 showed minimal, if any, bone formation and remained grossly unstable, prohibiting plate removal or advancement to a solid diet. Histomorphometric analysis at 6 months revealed that 68% of the group 1 implants were replaced by mineralized bone, whereas mineralized bone occupied less than 4% of the implants in groups 2 and 3. Biomechanical testing at 6 months revealed that the average bending strength of the reconstructed hemimandibles (expressed as a percentage of the contralateral hemimandible) was 27% for group 1 and 0% for group 2. The biomechanical strength of the defects reconstructed with BMP-2 increased significantly from 3 to 6 months and was related to degree of mineralization and thickness of bone bridging the defect.

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9/7/7 (Item 3 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00050814

Ocular Findings in Patients With Autosomal Dominant Retinitis Pigmentosa and a Rhodopsin Gene Defect (Pro-23-His) (Article)

Berson, Eliot L., MD; Rosner, Bernard, PhD; Sandberg, Michael A., PhD; Dryja, Thaddeus P. MD
Archives of Ophthalmology
1991; 109: 92 (9)
0003-9950

Ocular findings are presented from 17 unrelated patients with a form of autosomal dominant retinitis pigmentosa and the same cytosine-to-adenine transversion in codon 23 of the rhodopsin gene corresponding to a substitution of histodine for proline in the 23rd amino acid of rhodopsin (designated rhodopsin, Pro-23-His). On average, these patients (mean age, 37 years) had significantly better visual acuity and larger

electroretinographic amplitudes than 131 unrelated patients (mean age, 32 years) with autosomal dominant retinitis pigmentosa without this mutation. However, these 17 patients from separate families, as well as 12 relatives with the mutation from four of these families, showed interfamilial and intrafamilial variability with respect to severity of their ocular disease, suggesting that some factor(s) other than this gene defect itself is involved in the expression of their condition. This form of retinitis nigmentosa can now be detected by testing leukocyte DNA from peripheral blood. Some mechanisms by which this mutation in the rhodopsin gene could lead to rod photoreceptor cell death are suggested.

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9/7/8 (Item 4 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00039934
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Surgical Disease in East Africa; Presidential Address (PAPERS READ BEFORE THE 67TH ANNUAL MEETING OF THE NEW ENGLAND SURGICAL SOCIETY DIXVILLE NOTCH, NH, SEPT 26-28, 1986)

MCDERMOTT, WILLIAM V.
Archives of Surgery
April, 1987; 122: 397-402
LINE COUNT: 00411 WORD COUNT: 05683
ISSN: 0004-0010
CORPORATE SOURCE: Accepted for publication Dec 9, 1986. From the Department of Surgery, Harvard Medical School, and the New England Deaconess Hospital, Boston. Read as the Presidential Address before the 67th Annual Meeting of the New England Surgical Society, Dixville Notch, NH, Sept 27, 1986. Reprint requests to New England Deaconess Hospital, 110 Francis St, Boston, MA 02115 (Dr McDermott).

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

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9/7/9 (Item 5 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00039528
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The Boston Center for Liver Transplantation (BCLT); Initial Experience of a New Surgical Consortium (PAPERS READ BEFORE THE 66TH ANNUAL MEETING OF THE NEW ENGLAND SURGICAL SOCIETY, DIXVILLE NOTCH, NH, OCT 11-13, 1985)

JENKINS, ROGER L.
Archives of Surgery
April, 1986; 121: 424-430
LINE COUNT: 00310 WORD COUNT: 04290
ISSN: 0004-0010
CORPORATE SOURCE: Accepted for publication Jan 7, 1986. From the Department of Surgery, Harvard Medical School and New England Deaconess Hospital, Boston. Read before the 66th Annual Meeting of the New England Surgical Society, Dixville Notch, NH, Oct 12, 1985. Reprint requests to Department of Surgery, New England Deaconess Hospital, 185 Pilgrim Rd, Boston, MA 02215 (Dr Jenkins). Clinical membership of the Boston Center

for Liver Transplantation is as follows: Joseph p. Vacanti, MD, Robert C. Shamberger, MD, Craig W. Lillihei, MD, Raphael H. Levey, MD, and David H. Perlmutter, MD (Children's Hospital); Benedict A. Cosimi, MD, Francis L. Delmonico, MD, Paul S. Russell, MD, Patricia K. Donahoe, MD, Jules L. Deinstag, MD, and Ronald E. Kleinman, MD (Massachusetts General Hospital); Roger L. Jenkins, MD, Peter N. Benotti, MD, Albert Bothe, Jr, MD, Richard J. Rohrer, MD, William V. McDermott, Jr, MD, Anthony P. Monaco, MD, Thomas E. Dodson, MD, and Charles Trey, MD (New England Deaconess Hospital); Sang I. Cho, MD, Randolf B. Reinhold, MD, Alan W. Hackford, MD, Lucian L. Leape, MD, Burton H. Harris, MD, William C. Mackey, MD, Marshall M. Kaplan, MD, and Richard J. Grand, MD (New England Medical Center).

ABSTRACT: Improved survival following liver transplanatation has led to a rapid increase in the number of centers providing this expensive and demanding therapy. In January 1984, four Boston hospitals launched a cooperative program known as the Boston Center for Liver Transplantation (BCLT). From January 1984 through July 1985, 47 liver transplantations were performed in 41 patients ranging in age from 8 months to 60 years. Donor organs were retrieved from 22 states within a 2,500-mile radius. Thirty-five of the 47 procedures were performed by teams consisting of surgeons from at least two BCLT member hospitals. Twelve-month actuarial survival was 54.1% without significant institutional variability. The BCLT has developed into a unique transplant consortium capable of sharing manpower, equipment, and organs without sacrificing quality of care or disrupting preexisting medical services.

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

CITED REFERENCES:

Discussion

FRANCIS D. MOORE, MD, Boston: The liver consortium established in Boston has very little to be modest about and a great deal to be proud of! I think that their work is a great achievement, and surely one of its most interesting accomplishments is on the organizational/financial side. The efforts of Paul Russell, MD, and myself to have a cardiac transplantation consortium in the Boston hospitals has just within the last few days been crowned with assent because of the success of the BCLT.

The results of Dr Jenkins' group show 54% survival at one year. This figure will improve. And yet they are light-years ahead of our early efforts of almost 30 years ago. Since that was a New England surgical story, a brief account is fitting for a meeting of this Society; Dr Jenkins has kindly asked me if I would tell that story, however briefly.

In 1957, three years after the twin kidneys and five years before Joe Murray, MD, and Roy Calne, MD, introduced imuran, we undertook experimental liver transplantation in the dog with the scientific objective of determining the immunologic effect of an antigen overload. The liver was the largest organ you could transplant, but there was evidence that this procedure might produce immunologic paralysis. Our team was an interesting one, consisting of two New England surgeons, Brownie Wheeler, MD (now professor and Chief of the Department of Surgery at the University of Massachusetts), and Alan Birch, MD (now professor and Chief of the Department of Surgery at Southern Illinois University), and a surgeon from England, Dr Calne (now Chairman and Chief of the Department of Surgery at Cambridge). The operation that we worked out involved two low-pressure venovenous shunts to decompress the portal and systemic circuits when they were cross-clamped; we just assumed that this procedure would always be

necessary and we did not make any great fuss about it. The animal showed satisfactory surgical recovery, and when immunosuppressive chemotherapy was developed a few years later we could abate rejection. But that is not, and still is not, the only problem in liver transplantation. In fact, Dr Jenkins only had two rejection deaths.

About eight years after our first animal experiments, and with immunosuppressive chemotherapy well established in our department, Dr Birch and I operated on four patients, an experience we have never published in detail. The patients all suffered from terminal liver disease. There were two adults, of whom one was a male, basketball-playing, high school student with multicentric hepatoma, and two children with very extensive and hopeless biliary atresia. The patient who survived the longest lived for only eight weeks. Right or wrong, we decided that the time to operate had not yet come.

The canine operation we performed was essentially the same as that done now. The hepatic artery in the dog has extensive branching and is a nuisance: sometimes we anastomosed it end-to-side to the renal artery. I would just like to agree with Sir Rodney Smith that radical approaches to cancer of the upper abdomen usually do not pay off. It may interest you to know that all of the large liver transplant series have reported a few very good results in that particular disease.

Tom Starzl, MD, and I knew of our mutual interest in this field. We kept a close cooperative relationship throughout the years. His experience now sets the world standard. Dr Calne was working with Dr Murray on kidney transplantation, but he went back to Cambridge and rapidly developed an extensive experience in liver transplantation.

I would like to emphasize that it was on the basis of the work of Drs Calne and Starzl, and not our cautious efforts, that the later experience of Dr Jenkins and William McDermott, MD, and their group has been built. All that we can state is that we were early workers in the field and maybe gave a little strength of conviction and determination to two younger men, Drs Starzl and Calne, who went ahead and did the job so beautifully well.

Of the organ and tissue transplantations now performed, I believe that the liver is the most technically challenging and will always have a lower long-term rate of survival than that of organs like the kidney and heart, which have a simple blood supply and no bile to drain off. The low pressure circuits in the liver are what cause the trouble. It takes a master surgeon to perform this operation and to do it well, and Dr Jenkins has shown us all that we have such a liver transplanter now in New England. I am very proud of his work and very pleased to be asked to discuss it 30 years after we worked at the problem.

DR JENKINS: Thank you very much, Dr Moore. I do want to emphasize that this is not an individual effort and really has been a team effort from its inception. There are really a lot of people to thank, including Dr Moore, Dr McDermott, Dr Russell, and all the people who made this consortium work at the administrative level, as well as in the operating room. We also need to thank all of the people in the operating room and on the wards that helped to take care of these patients. They are many times the forgotten people.

9/7/10 (Item 6 from file: 442)
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00035019
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# Antibody-Dependent Cellular Cytotoxicity: Relation to Stage and Disease Course in North American Patients With Nasopharyngeal Carcinoma (PAPERS READ BEFORE THE AMERICAN SOCIETY FOR HEAD AND NECK SURGERY MEETING )

NEEL, H. BRYAN, III; PEARSON, GARY R.; TAYLOR, WILLIAM F.
Archives of Otolaryngology
November, 1984; 110: 742-747
LINE COUNT: 00281 WORD COUNT: 03878
ISSN: 0003-9977
CORPORATE SOURCE: Accepted for publication June 18, 1984. From the Departments of Otorhinolaryngology (Dr Neel), Immunology (Dr Pearson), and Medical Statistics and Epidemiology (Dr Taylor), Mayo Clinic and Mayo Foundation, Rochester, Minn. Read before the American Society for Head and Neck Surgery, Palm Beach, Fla, May 10, 1984. Reprint requests to Department of Otorhinolaryngology, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (Dr Neel). This investigation was supported in part by contract CP91006 from the Division of Cancer Cause and Prevention, National Cancer Institute, Bethesda, Md, and the St Jude Fund for Research and Education in Otolaryngology. Table 2 is reproduced with permission from the International Agency for Research on Cancer.

ABSTRACT: A prospective study of North American patients, mostly white, with different histopathologic types of nasopharyngeal carcinoma was initiated approximately five years ago. Several anti-Epstein-Barr virus (EBV) serologic tests are being evaluated; one is the antibody-dependent cellular cytotoxicity (ADCC) assay, which measures antibodies to an EBV-induced membrane antigen component. A low ADCC titer at diagnosis reflects a poor prognosis, and the determination of antibody titers by this assay identifies patients in whom recurrent disease is likely to develop after conventional radiation therapy for World Health Organization types 2 and 3 carcinomas. Of the patients who had high ADCC titers at diagnosis, 80% survived three years or longer, whereas 50% of the patients with low titers survived three years, and only 35% survived five years. High and low ADCC titers were seen in all stages (except in Ho stage V), and the distribution of patients by high and low ADCC titers was similar in each of the stage groupings. We conclude that the ADCC titer at the time of diagnosis is generally predictive of the prognosis.Clinical staging is the traditional approach for predicting prognosis, but determination of the ADCC titer can be used to segregate patients within the stage groups into those with "good" and "poor" prognoses. Serologic testing may eventually become one of the methods for staging patients with WHO types 2 and 3 nasopharyngeal carcinoma. (Arch Otolaryngol 1984; 110: 742-747)

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Sequestered Substernal Goiter (CLINICAL OBSERVATIONS)

LADENSON, PAUL W.; VINEYARD, GORDON C.; PINKUS, GERALDINE S.; RIDGWAY, E. CHESTER
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ABSTRACT: A young woman with a normally located and only subtly nodular thyroid gland in the neck was found to have a clinically distinct and radioisotopically "cold" anterior mediastinal mass, which proved to be a benign colloid adenoma. While this constellation of findings usually suggests the presence of a nonthyroidal neoplasm, eg, lymphoma, thymoma, or teratoma, our case illustrates that sequestered benign nodular goiter should also be considered in the differntial diagnosis. Clinical clues, such as a nodular thyroid gland, movement of the mass with deglutition, and a family history of nodular goiter, should suggest this possibility. A characteristic computed tomogrpahic appearance may also prove useful in recognition of this rare disorder. (Arch Intern Med 1983;143:1015-1017)

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# Treatment Of Refractory Disseminated Nontuberculous Mycobacterial Infection With Interferon Gamma A Preliminary Report (Original Articles)

Holland. Steven M.; Eisenstein, Eli M.; Kuhns, Douglas B.; Turner, Maria L.; Fleisher, Thomas A.; Strober, Warren; Gallin, John I.
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Abstract

Background. Studies conducted in vitro and in animals suggest that cytokine signals to monocytes or macrophages by interferon gamma are important in the containment and clearance of disseminated nontuberculous mycobacterial infections.

Methods. We studied seven patients with refractory disseminated nontuberculous mycobacterial infections who were not infected with the human immunodeficiency virus. Three patients were from a family predisposed to the development of Mycobacterium avium complex infections; four patients had idiopathic CD4+ T-lymphocytopenia. Their infections were culture- or biopsy-proved, involved at least two organ systems, and had been treated with the maximal tolerated medical therapy. Cellular proliferation, cytokine production, and phagocyte function were assessed in peripheral-blood cells. Interferon gamma was administered subcutaneously two or three times weekly in a dose of 25 to 50 microg per square meter of body-surface area in addition to antimycobacterial medications. Clinical effects were monitored by cultures, biopsies, radiographs, and in one patient a change in the need for paracentesis.

Results. In response to phytohemagglutinin, the production of interferon gamma by mononuclear cells from the patients was lower than in normal subjects ($P<0.001$), whereas stimulation with ionomycin and phorbol myristate acetate led to normal production of interferon gamma in the patients. Within eight weeks of the start of interferon gamma therapy, all seven patients had marked clinical improvement, with abatement of fever, clearing of many lesions and quiescence of others, radiographic improvement, and a reduction in the need for paracentesis.

Conclusions. Interferon gamma in combination with conventional therapy may be effective for some cases of refractory disseminated nontuberculous mycobacterial infection. (N Engl J Med 1994;330:1348-55.)

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# Weekly Clinicopathological Exercises: Case 1-1992: A 34-Year-Old Woman With Dyspnea And Multiple Small Cystic Areas In The Lungs (Case Records of the Massachusetts General Hospital)

Scully, Robert E.; Mark, Eugene, J.; McNeely, William F.; McNeely, Betty U.

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Medical Progress: Brain Tumors (second of Two Parts) (Review Articles)

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Case 7-1989: Unilateral Exophthalmos Three Years After Treatment Of Cervical And Mediastinal Hodgkin's Disease (Case Records of the Massachusetts General Hospital)

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Case 7-1988: A 27-Year-Old Man with Acute Myelomonocytic Leukemia in Remission and Repeated Intracranial Hemorrhages (Case Records of the Massachusetts General Hospital)

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Coronary artery bypass in patients with total laryngectomy

11/TI/40 (Item 19 from file: 73)
DIALOG(R)File 73:(c) 1994 Elsevier Science B.V. All rts. reserv.

Radiology of large transincisural masses

11/TI/41 (Item 20 from file: 73)
DIALOG(R)File 73:(c) 1994 Elsevier Science B.V. All rts. reserv.

Breakaway safety feature for an intra-oral cone system

11/TI/42 (Item 21 from file: 73)
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Ultrastructural localization of acid phosphatase in immunologically defined neoplastic lymphocytic cells and hairy cells. A comparison between two different substrates

11/TI/43 (Item 22 from file: 73)
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Primary choroid plexus papilloma of the cerebellopontine angle

11/TI/44 (Item 23 from file: 73)
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Extra-cranial tumours of the infratemporal fossa

11/TI/45 (Item 24 from file: 73)
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Normal intramammary lymph nodes presenting as occult breast masses

11/TI/46 (Item 25 from file: 73)
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Electromyographic evidence of inferior gluteal nerve compromise: An early representation of recurrent colorectal carcinoma

11/TI/47 (Item 26 from file: 73)
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Malignant ameloblastoma with metastasis to the skull: Report of case

11/TI/48 (Item 27 from file: 73)
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Transcutaneous continuous wave Doppler ultrasound in the diagnosis of left atrial myxoma

11/TI/49 (Item 28 from file: 73)
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Facial reflex examination. A clinical and neurophysiological study on acoustic tumours and brain displacement at the tentorial notch

11/TI/50 (Item 29 from file: 73)
DIALOG(R)File 73:(c) 1994 Elsevier Science B.V. All rts. reserv.

M-mode echocardiography in the detection of intracardiac tumors
M-MODE ECHOKARDIOGRAPHIE BEI INTRAKARDIALEN TUMOREN
?

4/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1994 BIOSIS. All rts. reserv.

6404069 BIOSIS Number: 85004590
THE EFFECT OF PRESTAINING PRIOR TO IMMUNOREACTION DURING ELECTROPHORETIC BLOTTING OF PROTEINS
TRACY R P; MONKOVIC D; ANDRIANORIVO A; CALORE J; MACKAY A
DEP. PATHOL., HEALTH SCI. COMPLEX, UNIV. VT., BURLINGTON, VT.05405, USA.
ELECTROPHORESIS 8 (8). 1987. 350-355. CODEN: ELCTD
Full Journal Title: Electrophoresis
Language: ENGLISH
We have used six different monoclonal and polyclonal antibodies, four different antigen preparations and two different detection systems to compare Western blotting with Coomassie Blue prestained gels (Jackson and Thompson, Electrophoresis, 1984, 5, 35-42) to blotting of unstained gels with Amido Black or Fast Green post-transfer staining of the nitrocellulose. Contrary to a recent report (Harper et al., Anal. Biochem., 1986, 157, 270-274), in which post-staining with Coomassie Blue was determined to severely inhibit immunoreactivity, we find using prestained Coomassie Blue gels to be extremely useful in most cases, although, rarely, inhibition of the immune reaction may take place. Post-staining with Amido Black or Fast Green may also prove useful, but is not recommended since similar inhibition occurs, and there are the addeded disadvantages of not being able to "pre-view" the gel pattern and not being able to use stored gels. Further studies indicated that the rare loss of immunoreactivity seen with Coomassie Blue prestained gels is most likely due to the necessary fixation step, and not the stain itself (as has been suggested), since the protein-dye complex is dissociated during transfer.

4/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1994 BIOSIS. All rts. reserv.

5234529 BIOSIS Number: 81001836
A SENSITIVE ASSAY OF CYTOTOXICITY APPLICABLE TO MIXED CELL POPULATIONS
DUERST R E; FRANTZ C N
DEP. PEDIATRICS, UNIV. ROCHESTER SCH. MED. AND DENTISTRY, ROCHESTER, N.Y. 14642, USA.
J IMMUNOL METHODS 82 (1). 1985. 39-46. CODEN: JIMMB
Full Journal Title: Journal of Immunological Methods
Language: ENGLISH
The fluorescent vital dye, Hoechst 33342, was used to stain cultured cells prior to assay of antibody dependent complement mediated cytotoxicity. The fluorescence of nonviable dye stained cell is quenched by cellular uptake of trypan bue, but trypan blue excluding cells remain intensely fluorescent. Detection by fluorescence microsocpy of one viable prestained cell per 105 unstained cells was accurate and reliable. The technique was found to have sensitivity equal to a clonogenic assay for measuring cytotoxicity. The dye stained cell assay may be used to measure depletion of a selected cell type, when those cells are stained prior to mixing with another cell population. This technique may prove useful to

study model systems for depletion of tumor cells or T-cells from bone marrow.

4/7/20 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE
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103452 EMBASE No: 74105173
Nitroblue tetrazolium. A new lipoprotein stain
Segal A.W.; Putman D.; Minchin Clarke H.G.
Clin. Res. Cent., Harrow UNITED KINGDOM
ATHEROSCLEROSIS (AMST.) (NETHERLANDS) , 1973, 18/3 (499-504) CODEN: ATHSB
LANGUAGES: ENGLISH
The diformazan of nitroblue tetrazolium (NBT) is presented as a new, specific pre stain for lipoproteins. NBT requires no organic solvent and is shown to be effective in agarose, cellulose acetate and polyacrylamide gel. When added in the correct concentrations, NBT does not appear to alter the electrophoretic migration or antigen antibody reaction of the lipoproteins.

4/7/21 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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07308891 90215891
Coomassie brilliant blue R-250 as a highly sensitive pre-stain for immediate visualization of human serum proteins on polyacrylamide gel disc electrophoresis and raising monospecific antibodies.
Saoji AM; Kulkarni M; Naghi T
Indian J Pathol Microbiol (INDIA) Oct 1989, 32 (4) p286-90, ISSN 0377-4929 Journal Code: GKK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
We hereby describe electrophoretic analysis of normal human serum pre-stained with Coomassie Brilliant Blue R-250 (CBB). The proposed method was optimized by studying as many as 450 disc electrophoretic separations and 30 variables. The method when compared with the post-electrophoretic staining by Amido Black (AB) revealed that the pre-stained discs were intensely well defined and resolved within 2 hours with a transparent gel. Gels stained with AB, despite a prolonged destaining, showed a residual dye retention making identification of the faint components difficult. Protein eluted from the CBB pre-stained gels retained its purity and immunoreactivity and conjugates of the two prototype proteins namely the albumin and the transferrin produced high-titre monospecific antisera in immunized rabbits.

4/7/22 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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07077326 89379326
Identification of C-3 on polyacrylamide gel by pre-staining the normal human ser[redacted]l Brilliant Blue and raising monospecific anti C-3

antibody.

Saoji AM; Naghi T
Indian J Pathol Microbiol (INDIA) Jul 1989, 32 (3) p221-6, ISSN 0377-4929 Journal Code: GKK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Based on our earlier work we hereby describe pre-staining of normal human serum with Remazol Brilliant Blue (RBB) to precisely locate the third component of complement system (C3,B1C) on polyacrylamide gels. Testing the dye-protein complex eluted from different immunoreactive post-transferrin (origin to transferrin) components against the standards anti-C3 antibody in various gel precipitation techniques, revealed that the prominent band just posterior to the centrally placed transferrin is of complement. Subsequent to its identity, we also evolved a method to raise an anti-C3 antibody. The resulting antibody was found to be monospecific when assessed in different gel precipitation procedures.

4/7/29 (Item 3 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00046604
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Intralaboratory Quality Assurance of Immunohistochemical Procedures; Recommended Practices for Daily Application ( COLLEGE OF AMERICAN PATHOLOGISTS CONFERENCE XV AUGUST 22-24, 1988)

RICKERT, ROBERT R.
Archives of Pathology and Laboratory Medicine
June, 1989; 113: 673-679
LINE COUNT: 00422 WORD COUNT: 05824
ISSN: 0363-0153
CORPORATE SOURCE: Accepted for publication Oct 13, 1988. From the Department of Pathology, St. Barnabas Medical Center, Livingston, NJ. Reprint requests to Department of Pathology, St Barnabas Medical Center, Old Short Hills Road, Livingston, NJ 07039 (Dr Rickert).

ABSTRACT: During the past several decades, immunohistologic techniques have been developed that may provide important adjunctive information to the diagnostic pathologist. These procedures are now widely available and commonly used in the pathology laboratory. Proper performance of immunohistochemical procedures and interpretation of their results require development and implementation of appropriate quality control and quality assurance measures. This article reviews the application of quality control standards in the immunohistochemistry laboratory and the integration of these activities into the overall quality assurance program of the department.

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

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specificity. J Histochem Cytochem 1983;31:691-696.

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apparent effects, overexpression of activated Notch in the same cells transiently blocks their proper cell-fate commitment, causing them to either adopt incorrect cell fates or to differentiate incompletely. Moreover, an activated Notch protein lacking the transmembrane domain is translocated to the nucleus, raising the possibility that Notch may participate directly in nuclear events.

15/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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10805885 BIOSIS Number: 97005885
An activated notch receptor blocks cell-fate commitment in the developing Drosophila eye
Fortini M E; Rebay I; Caron L A; Artavanis-Tsakonas S
Dep. Cell Biol., Yale Univ., New Haven, CT 06536, USA
Nature (London) 365 (6446). 1993. 555-557.
Full Journal Title: Nature (London)
ISSN: 0028-0836
Language: ENGLISH
The Notch locus of Drosophila melanogaster encodes a 2,703-amino-acid transmembrane protein required for a variety of developmental processes, including neurogenesis, oogenesis and ommatidial assembly. The Notch protein contains a large extracellular domain of 36 epidermal growth factor-like repeats as well as three Notch/Lin-12 repeats and an intracellular domain with 6 Cdc10/ankyrin repeats, motifs that are highly conserved in several vertebrate Notch homologues. Truncation of the extracellular domain of the Drosophila Notch protein produces an activated receptor, as judged by its ability to cause phenotypes similar to gain-of-function alleles or duplications of the Notch locus. Equivalent truncations of vertebrate Notch-related proteins have been associated with malignant neoplasms and other developmental abnormalities. We present here an analysis of activated Notch function at single-cell resolution in the Drosophila compound eye. We find that overexpression of full-length Notch in defined cell types has no apparent effects but that overexpression of activated notch in the same cells transiently blocks their proper cell-fate commitment, causing them either to adopt incorrect cell fates or to differentiate incompletely. Moreover, an activated notch protein lacking the transmembrane domain is translocated to the nucleus, raising the possibility that Notch may participate directly in nuclear events.

15/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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10110234 BIOSIS Number: 95110234
DLK A PUTATIVE MAMMALIAN HOMEOTIC GENE DIFFERENTIALLY EXPRESSED IN SMALL CELL LUNG CARCINOMA AND NEUROENDOCRINE TUMOR CELL LINE
LABORDA J; SAUSVILLE E A; HOFFMAN T; NOTARIO V
CENTER BIOL. RESEARCH, FDA., 8800 ROCKVILLE PIKE, BLDG. 29, BETHESDA, MD 20892, USA.
J BIOL CHEM 268 (6). 1993. 3817-3820. CODEN: JBCHA
Full Journal Title: Journal of Biological Chemistry
Language: ENGLISH

Gastrin releasing peptide is mitogenic for mouse Swiss 3T3 fibroblasts and certain human small cell lung carcinoma (SCLC) cells but not for mouse Balb/c 3T3 fibroblasts. To identify new molecules associated with the gastrin releasing peptide-responsive phenotype, clones isolated from a differential cDNA library between Swiss and Balb/c 3T3 fibroblasts were used to screen for their expression in human SCLC cell lines. Using this approach, we have isolated and characterized human and mouse cDNA clones encoding a novel protein. This protein is a putative transmembrane protein belonging to the epidermal growth factor-like superfamily. In vitro transcription and translation studies detect a 42-kDa protein, in agreement with the size predicted from the translated cDNA sequence. This protein (termed Delta-like or dlk) is highly homologous to invertebrate homeotic proteins, including Delta, and Notch, the products of neurogenic loci involved in normal neural differentiation in Drosophila. dlk is expressed in tumors with neuroendocrine features, such as neuroblastoma, pheochromocytoma, and a subset of SCLC cells lines. However, its expression in normal tissues is restricted to the adrenal gland and placenta. These data suggest that dlk may be involved in neuroendocrine differentiation and, because of its cellular location and restricted expression in normal tissues, it may be a potential therapeutic target in neuroendocrine tumors, particularly SCLC.

15/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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9590824 BIOSIS Number: 94095824
EXPRESSION PATTERN OF MOTCH A MOUSE HOMOLOG OF DROSOPHILA NOTCH SUGGESTS AN IMPORTANT ROLE IN EARLY POSTIMPLANTATION MOUSE DEVELOPMENT
FRANCO DEL AMO F; SMITH D E; SWIATEK P J; GENDRON-MAGUIRE M; GREENSPAN R J; MCMAHON A P; GRIDLEY T
DEP. CELL DEVELOPMENTAL BIOL., ROCHE INST. MOLECULAR BIOLOGY, ROCHE RES. CENTER, NUTLEY, NJ 07110.
DEVELOPMENT (CAMB) 115 (3). 1992. 737-744. CODEN: DEVPE
Full Journal Title: DEVELOPMENT (Cambridge)
Language: ENGLISH
The Notch gene of Drosophila encodes a large transmembrane protein involved in cell-cell fate decisions in the Drosophila embryo. To determine if a gene homologous to Drosophila Notch plays a role in early mouse development, we screened a mouse embryo cDNA library with probes from the Xenopus Notch homolog, Xotch. A partial cDNA clone encoding the mouse Notch homolog which we have termed Motch, was used to analyze expression of the Motch gene. Motch transcripts were detected in a wide variety of adult tissues, hich included derivatives of all three germ layers. Differentiation of P19 embryonal carcinoma cells into neuronal cell types resulted in increased expression of Motch RNA. In the postimplantation mouse embryo Motch transcripts were first detected in mesoderm at 7.5 days post coitum (dpc). By 8.5 dpc, transcript levels were highest in presomitic mesoderm, mesenchyme and endothelial cells, while much lower levels were detected in neuroepithelium was a major site of Motch expression. Transcripts were also abundant in cell types derived from neural crest. These data suggest that the Motch gene plays multiple roles in patterning and differentiation of the early postimplantation mouse embryo.

15/7/7 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal
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10278296 PASCAL No.: 92-0484208
Expression pattern of Motch, a mouse homolog of Drosophila notch, suggests an important role in early postimplantation mouse development
DEL AMO F F; SMITH D E; SWIATEK P J; GENDRON-MAGUIRE M; GREENSPAN R J; MCMAHON A P; GRIDLEY T
Roche inst. molecular biology, dep. cell developmental biology, Nutley NJ 07110, USA
Journal: Development : (Cambridge), 1992, 115 (3) 737-744
ISSN: 0950-1991 Availability: INIST-7560; 354000020190410090
No. of Refs.: 1 p.1/2
Document Type: P (Serial) ; A (Analytic)
Country of Publication: United Kingdom
Language: English
The Notch gene of Drosophila encodes a large transmembrane protein involved in cell-cell interactions and cell fate decisions in the Drosophila embryo. To determine if a gene homologous to Drosophila Notch playis a role in early mouse development, we screened a mouse embryo cDNA library with probes from the Xenopus Notch homolog, Xotch. A partial cDNA clone encoding the mouse Notch homolg, which we have termed Motch, was used to analyze expression of the Motch gene. Motch transcripts were detected in a wide variety of adult tissues, which included derivatives of all three germ layers

15/7/8 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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09041700 94356700
Analysis of phenotypic abnormalities and cell fate changes caused by dominant activated and dominant negative forms of the Notch receptor in Drosophila development.
Rebay I; Fortini ME; Artavanis-Tsakonas S
Howard Hughes Medical Institute, Department of Cell Biology, Yale University, New Haven, Connecticut 06536-0812.
C R Acad Sci III (FRANCE) Sep 1993, 316 (9) p1097-123, ISSN 0764-4469 Journal Code: CA1
Languages: ENGLISH, FRENCH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, TUTORIAL
The Notch gene of Drosophila plays an important role in cell fate specification throughout development. The Notch protein contains a large extracellular domain of 36 EGF-like repeats as well as 3 Notch/lin-12 repeats and an intracellular domain with 6 cdc10/ankyrin repeats, motifs which are highly conserved in several vertebrate Notch homologues [1-7]. In this review we summarize the results of two recent studies which attempt to establish structure-function relationships of the various domains of the Notch gene product [8, 9]. The functions of various structural domains of the Notch protein in vivo were investigated using a series of deletion mutants which have been ectopically expressed either under the hsp70 heat-shock promoter or under the sevenless eye-specific promoter. Truncation of the extracellular domain of Drosophila Notch produces an activated receptor as judged by its ability to cause phenotypes matching

those of gain-of-function alleles or duplications of the Notch locus [8]. Equivalent truncations of vertebrate Notch-related proteins have been associated with malignant neoplasms and other developmental abnormalities [3, 6, 10, 11]. In contrast, dominant negative phenotypes result from overexpression of a protein lacking most intracellular sequences. These results were extended by an analysis of activated Notch function at single-cell resolution in the Drosophila compound eye [9]. It was shown that while overexpression of full-length Notch in defined cell types has no apparent effects, overexpression of activated Notch in the same cells transiently blocks their proper cell-fate commitment, causing them to either adopt incorrect cell fates or to differentiate incompletely. Moreover, an activated Notch protein lacking the transmembrane domain is translocated to the nucleus, raising the possibility that Notch may participate directly in nuclear events. (68 Refs.)

15/7/9 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1994 Dialog Info.Svcs. All rts. reserv.

06701790 89003790
Expression of the differentiation antigen F7D6 in tumorous tissues of Drosophila.
Bedian V; Jungklaus CE
Department of Biology, Clarkson University, Potsdam, New York 13676.
Dev Genet (UNITED STATES) 1987, 8 (3) p165-77, ISSN 0192-253X
Journal Code: DEG
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The 63-kDa antigen recognized by the monoclonal antibody F7D6 is present in all Drosophila embryonic cells and disappears from most tissues as each one reaches its final, differentiated state. Larval tissues lose the antigen around the time of hatching, imaginal tissues lose it during metamorphosis, and germ cells lose it during gametogenesis (Bedian et al: Devel Biol 115:105-118, 1986). The nervous system and spontaneously contracting musculature of the gut and gonads are exceptions and remain antigen positive at all stages. The F7D6 antigen appears to be associated with dividing, undifferentiated cells and electrogenic cells. This prompted us to test tumors for antigen presence. We tested four different recessive mutants that give rise to four different types of tumorous transformation: the embryonic tumor Notch, several larval melanotic tumors, the imaginal disc tumor 1(2)gl, and three alleles of the ovarian tumor otu. In all cases, tumorous tissues in homozygotes contained the F7D6 antigen. The electrophoretic mobility of the antigen appeared to be unaltered in tumorous tissues compared to normal cells, but the antigen is expressed at higher levels. The antigen is found on the cytoplasmic surface of plasma membranes and appears to be a marker of undifferentiated normal and tumorous cells. Similarities and differences between the F7D6 antigen and Drosophila c-src protein are discussed.

15/7/10 (Item 1 from file: 351)
DIALOG(R)File 351:DERWENT WPI
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009855324 WPI Acc No: 94-135180/16

XRAM Acc No: C94-062475
XRPX Acc No: N94-106287
Notch protein and nuclear acid compositions - is used for treatment of disorders of cell fate or differentiation esp. breast, colon or cervical cancer
Patent Assignee: (UYYA ) UNIV YALE
Author (Inventor): ARTAVANIS-TSAKONAS S; BLAUMUELLER C M; FEHON R G; ZAGOURAS P
Number of Patents: 002
Number of Countries: 045
Patent Family:

| CC | Number | Kind | Date | Week | |
|---|---|---|---|---|---|
| WO | 9407474 | A1 | 940414 | 9416 | (Basic) |
| AU | 9453503 | A | 940426 | 9432 | |

Priority Data (CC No Date): US 955012 (920930); US 83590 (930625)
Applications (CC,No,Date): AU 9453503 (930930); WO 93US9338 (930930)
Language: English
EP and/or WO Cited Patents: 6.Jnl.Ref; US 5115096; US 5132212; US 5264557
Designated States
(National): AU; BB; BG; BR; BY; CA; CZ; FI; HU; JP; KP; KZ; LK; LV; MG; MN ; MW; NO; NZ; PL; RO; RU; SD; SK; UA; US; UZ; VN
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LU; MC; NL; OA; PT ; SE
Filing Details: AU9453503 Based on WO 9407474
Abstract (Basic): WO 9407474 A
The pharmaceutical compsn. comprises a therapeutically effective amt. of a Notch protein (A) and a pharmaceutically acceptable carrier.
USE - The compsns. can be used for treatment of disorders of cell fats or differentiation. The therapeutic compsns. include Notch proteins and analogues, derivs. and fragments, antibodies, nucleic acid encoding, analogues and derivs., Notch antisense nucleic acids, toporythmic proteins and derivs. which bind or interact with Notch proteins, their encoding nucleic acids or Abs. The compsn. is pref. admin. to a cancerous condition, e.g. breast, colon or cervical cancer, or to prevent progression from a pre-neoplastic or non-malignant state into a neoplastic or malignant state. Dwg.0/17
Derwent Class: B04; D16; S03;
Int Pat Class: A61K-031/70; A61K-037/02; A61K-039/395; A61K-039/44; C07H-021/04; G01N-033/53; G01N-033/68

15/7/11 (Item 2 from file: 351)
DIALOG(R)File 351:DERWENT WPI
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009400489 WPI Acc No: 93-093998/11
XRAM Acc No: C93-041615
DNA encoding GA binding protein sub-unit - allows investigation of sub-unit sequence motif functions, for control of rapid cell division e.g. in cancer; GUANOSINE ADENOSINE PURINE
Patent Assignee: (CARN-) CARNEGIE INSTITUTION WASHINGTON; (CARN-) CARNEGIE INST WASHINGTON
Author (Inventor): LAMARCO K L; MCKNIGHT S L; THOMPSON C C
Number of Patents: 003
Number of Countries: 019

Patent Family:

| CC Number | Kind | Date | Week | |
|---|---|---|---|---|
| WO 9304166 | A1 | 930304 | 9311 | (Basic) |
| AU 9224857 | A | 930316 | 9328 | |
| EP 598839 | A1 | 940601 | 9421 | |

Priority Data (CC No Date): US 746032 (910816)
Applications (CC,No,Date): EP 92918552 (920817); WO 92US6748 (920817); WO 92US6748 (920817); AU 9224857 (920817)
Language: English
EP and/or WO Cited Patents: 19Jnl.Ref; WO 8909777; WO 9005745; WO 9107423
Designated States
(National): AU; CA; JP
(Regional): AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT; LI; LU; MC; NL; SE
Filing Details: EP0598839 Based on WO 9304166; AU9224857 Based on WO 9304166
Abstract (Basic): WO 9304166 A

DNA encoding a GA binding protein (GABP) subunit, or an epitope specific, to it or a DNA fragment complementary to this DNA is new. Also claimed are: (1) a recombinant DNA molecule comprising the DNA segment and a vector; and (2) a host cell transformed with the DNA of (1).

GABP alpha has a 454 aminoacid sequence and GABP beta 1 has a 382 aminoacid sequence (both given in the specification). GABP is produced by culturing the transformed cells.

USE - The DNA encodes the subunits GABP alpha, GABP beta 1 or GABP beta 2, or portions of these. GABP alpha is related to the Ets transforming protein, and GABP beta contains a series of 33 aminoacid repeats related to, e.g. Notch of Drosophila melanogaster, Lin12 and Glp1 of Caenorhabditis elegans and SW14 and SW16 of Saccharomyces cerevisiae. These 2 protein sequence motifs contribute to the surfaces that form a multiprotein complex capable of stable and specific interaction with DNA. DNA sequences encoding these motifs may therefore be useful in investigating the problems of regulatory specificity, and may help define a discrete function for the 33 aminoacid repeat motifnsf Dwg.0/13

Derwent Class: B04; D16;
Int Pat Class: C12N-015/12; C12N-015/63; C12N-015/70; C12N-015/74; C12N-015/79

15/7/12 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs
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164909 DBA Accession No.: 94-07460 PATENT
Notch protein and antisense DNA - application in carcinoma diagnosis, therapy and gene therapy
PATENT ASSIGNEE: Univ.Yale 1994
PATENT NUMBER: WO 9407474 PATENT DATE: 940414 WPI ACCESSION NO.: 94-135180 (9416)
PRIORITY APPLIC. NO.: US 83590 APPLIC. DATE: 930625
NATIONAL APPLIC. NO.: WO 93US9338 APPLIC. DATE: 930930
LANGUAGE: English
ABSTRACT: A pharmaceutical composition comprising a Notch protein (A) and a carrier is claimed. More specifically, the composition comprises a

human Notch protein encoded by a specified DNA sequence which is bound by an antibody to a Notch protein. The following are also claimed: (1) a pure human Notch protein homolog of specified protein sequence; (2) nucleic acid encoding the protein of (1); (3) a recombinant cell containing the nucleic acid of (2); (4) a composition comprising a Notch protein or derivative (e.g. chimeric protein); (5) a composition comprising a molecule which antagonizes the function of a Notch protein; and (6) the use of the composition of (5) for treatment of cervix carcinoma, mamma carcinoma or colon carcinoma. In (4), the chimeric protein may include functionally active portions of the Notch protein encoded by human cDNA contained in plasmid phN3k (ATCC 68609) and plasmid phN5k (ATCC 68611). The therapeutic composition includes Notch proteins and analogs, antibodies, nucleic acid encoding the analogs, antisense nucleic acids, etc. which bind and interact with Notch proteins, their encoding nucleic acids or antibodies. (232pp)

15/7/13 (Item 1 from file: 399)
DIALOG(R)File 399:CA Search(R)
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121026887 CA: 121(3)26887m PATENT
Therapeutic and diagnostic methods and compositions based on Notch proteins and nucleic acids
INVENTOR(AUTHOR): Artavanis-Tsakonas, Spyridon; Fehon, Richard Grant; Zagouras, Panayiotis; Blaumueller, Christine Marie
LOCATION: USA
ASSIGNEE: Yale University
PATENT: PCT International ; WO 9407474 A1 DATE: 940414
APPLICATION: WO 93US9338 (930930) *US 955012 (920930) *US 83590 (930625)
PAGES: 232 pp. CODEN: PIXXD2 LANGUAGE: English CLASS: A61K-031/00A; A61K-031/70B; A61K-037/02B; A61K-039/44B; A61K-039/395B; C07H-021/04B; G01N-033/53B; G01N-033/68B DESIGNATED COUNTRIES: AU; BB; BG; BR; BY; CA; CZ; FI; HU; JP; KR; KZ; LK; LV; MG; MN; MW; NO; NZ; PL; RO; RU; SD; SK; UA; US; UZ; VN DESIGNATED REGIONAL: AT; BE; CH; DE; DK; ES; FR; GB; GR; IE; IT ; LU; MC; NL; PT; SE; BF; BJ; CF; CG; CI; CM; GA; GN; ML; MR; NE; SN; TD; TG
SECTION:
CA201006 Pharmacology
CA209XXX Biochemical Methods
IDENTIFIERS: human Notch protein therapeutic, cDNA antibody human Notch
DESCRIPTORS:
Gene,animal...
cDNA, for human Notch protein and Drosophila Delta protein
Deoxyribonucleic acid sequences,complementary...
for human Notch protein and Drosophila Delta protein
Alopecia... Cirrhosis... Intestine,neoplasm, colon, inhibitors... Keloid... Lung,neoplasm, inhibitors... Mammary gland,neoplasm, inhibitors... Neoplasm inhibitors,colon... Neoplasm inhibitors,lung... Neoplasm inhibitors,mammary gland... Neoplasm inhibitors,melanoma... Psoriasis...
Notch protein as diagnosistics and
Proteins,specific or class, gene Delta...
Notch protein as therapeutics in relation to
Deoxyribonucleic acids,complementary, antisense...
of human Notch gene, for diagnostics and therapeutics
Protein sequences...

of human Notch protein and Drosophila Delta protein
Gene,animal, Serrate...
protein of, Notch protein as therapeutics in relation to
Antibodies... Antibodies,monoclonal...
to human Notch protein, for diagnostics and therapeutics
Testis,neoplasm, seminoma... Uterus,neoplasm, cervix...
treatment and diagnosis of, Notch protein as diagnosistics and
CAS REGISTRY NUMBERS:
146636-21-7 amino acid sequence of
156067-46-8 156067-47-9 156067-48-0 156067-49-1 156067-50-4
156067-51-5 amino acid sequence of, therapeutics contg.
146636-19-3 human Notch protein homologous to, as therapeutics
148513-28-4 156067-52-6 156067-53-7 156067-54-8 156067-55-9 nucleotide
sequence of
146636-08-0 146636-13-7 156067-43-5 156067-44-6 156067-45-7 nucleotide
sequence of, therapeutics contg. protein encoded by

15/7/14 (Item 2 from file: 399)
DIALOG(R)File 399:CA Search(R)
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118184969 CA: 118(19)184969g JOURNAL
Mouse mammary tumor gene int-3: a member of the notch gene family
transforms mammary epithelial cells
AUTHOR(S): Robbins, Joan; Blondel, Bruno J.; Gallahan, Daniel; Callahan,
Robert
LOCATION: Lab. Tumor Immunol. Biol., Natl. Cancer Inst., Bethesda, MD,
20892, USA
JOURNAL: J. Virol. DATE: 1992 VOLUME: 66 NUMBER: 4 PAGES: 2594-9
CODEN: JOVIAM ISSN: 0022-538X LANGUAGE: English
SECTION:
CA203004 Biochemical Genetics
CA213XXX Mammalian Biochemistry
IDENTIFIERS: mouse mammary tumor gene int3 transformation, epithelium
transformation mouse notch like gene
DESCRIPTORS:
Epithelium...
cell, of mammary gland of mouse, gene int-3 transformation of
Deoxyribonucleic acid sequences...
for gene int-3 protein of mouse mammary tumor
Proteins,specific or class, gene int-3...
gene for, of mouse mammary tumor, sequence of and epithelial cell
transformation by
Virus,animal, murine mammary tumor...
gene int-3 integration site for, sequence of and epithelial cell
transformation by
Mouse...
gene int-3 of mammary tumor of, sequence of and epithelial cell
transformation by
Gene,animal, Notch...
mouse mammary tumor gene int-3 like, of Drosophila melanogaster,
sequence of and epithelial cell transformation by
Mammary gland,neoplasm...
notch family gene int-3 of mouse, sequence of and epithelial cell
transformation by

Drosophila melanogaster...
notch gene of, mouse mammary tumor gene int-3 as member of family of, sequence of and epithelial cell transformation by
Protein sequences...
of gene int-3 protein, of mouse mammary tumor
Gene,animal, int-3...
of mouse mammary tumor, sequence of and epithelial cell transformation by
Deoxyribonucleic acids,repetitive...
Saccharomyces cerevisiae cell cycle gene cdc-10 homolog, in gene int-3 of mouse mammary tumor
CAS REGISTRY NUMBERS:
146991-60-8 amino acid sequence of, complete
139861-79-3 nucleotide sequence of

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15/7/15 (Item 1 from file: 434)
DIALOG(R)File 434:SCISEARCH(R)
(c) 1994 Inst for Sci Info. All rts. reserv.

13463041 Genuine Article#: PP811 Number of References: 62
Title: DELAMINATION AND DIVISION IN THE DROSOPHILA NEURECTODERM - SPATIOTEMPORAL PATTERN, CYTOSKELETAL DYNAMICS, AND COMMON CONTROL BY NEUROGENIC AND SEGMENT POLARITY GENES
Author(s): HARTENSTEIN V; YOUNOSSIHARTENSTEIN A; LEKVEN A
Corporate Source: UNIV CALIF LOS ANGELES,DEPT BIOL/LOS ANGELES//CA/90024
Journal: DEVELOPMENTAL BIOLOGY, 1994, V165, N2 (OCT), P480-499
ISSN: 0012-1606
Language: ENGLISH Document Type: ARTICLE
Abstract: Cytoskeletal changes occurring during the delamination of precursors of the peripheral (microchaete precursors in the pupal notum) and central nervous system (embryonic SI neuroblasts) were studied. The pattern of cell division in the ventral neurectoderm (VN) of wild-type embryos was analyzed using BrdU incorporation and correlated to the pattern of neuroblast delamination. Finally, defects in the pattern of proliferation of the VN and neuroblast delamination which occur in Notch and wingless mutant embryos were described. The results indicate that the patterns of delamination and mitosis are closely correlated: delamination occurs either immediately after a cell has divided (in case of microchaete precursors) or shortly before the division (in case of the neuroblasts). In addition, cytoskeletal changes similar to those occurring during mitosis can be seen in delaminating neuronal precursors. Thus, during both mitosis and delamination, the discrete apicobasally oriented microfilament-tubulin bundles break down. Microfilaments form a dense, diffuse cortical layer surrounding the entire cell body. Microtubules are concentrated at the apically located centrosome. The relationship between mitosis and delamination is supported by the finding that the neurogenic gene Notch and segment polarity gene wingless (wg) affect both proliferation and delamination in the ventral neurectoderm. Thus, in embryos expressing the trunkated cytoplasmic domain of the neurogenic gene Notch under heat-shock control (Struhl et al., 1993), all ventral neurectodermal cells go into mitosis prematurely, followed by the absence of neuroblast delamination. In wg loss-of-function mutants, mitosis in the VN is irregular and generally postponed, accompanied by irregularities in the timing of neuroblast delamination in general and the absence of

a subset of neuroblasts. (C) 1994 Academic Press, Inc.

15/7/16 (Item 2 from file: 434)
DIALOG(R)File 434:SCISEARCH(R)
(c) 1994 Inst for Sci Info. All rts. reserv.

13393826 Genuine Article#: PK060 Number of References: 48
Title: 3 GENES IN THE HUMAN MHC CLASS-III REGION NEAR THE JUNCTION WITH THE CLASS-II - GENE FOR RECEPTOR OF ADVANCED GLYCOSYLATION END-PRODUCTS, PBX2 HOMEOBOX GENE AND A NOTCH HOMOLOG, HUMAN COUNTERPART OF MOUSE MAMMARY-TUMOR GENE INT-3
Author(s): SUGAYA K; FUKAGAWA T; MATSUMOTO K; MITA K; TAKAHASHI E; ANDO A; INOKO H; IKEMURA T
Corporate Source: NATL INST GENET,DEPT EVOLUTIONARY GENET,YATA 1111/MISHIMA/SHIZUOKA 411/JAPAN/; NATL INST GENET,DEPT EVOLUTIONARY GENET/MISHIMA/SHIZUOKA 411/JAPAN/; GRAD UNIV ADV STUDIES/MISHIMA/SHIZUOKA 411/JAPAN/; NATL INST RADIOL SCI/ANAGAWA/CHIBA 263/JAPAN/; TOKAI UNIV,SCH MED/ISEHARA/KANAGAWA 25911/JAPAN/
Journal: GENOMICS, 1994, V23, N2 (SEP 15), P408-419
ISSN: 0888-7543
Language: ENGLISH Document Type: ARTICLE
Abstract: Cosmid walking of about 250 kb from MHC class III gene CYP21 to class II was conducted. The gene for receptor of advanced glycosylation end products of proteins (RAGE, a member of immunoglobulin superfamily molecules), the PBX2 homeobox gene designated HOX12, and the human counterpart of the mouse mammary tumor gene int-3 were found. The contiguous RAGE and HOX12 genes were completely sequenced, and the human int-3 counterpart was partially sequenced and assigned to a Notch homolog. This human Notch homolog, designated NOTCH3, showed both the intracellular portion present in the mouse int-3 sequence and the extracellular portion absent in the int-3. It thus corresponds to the intact form of a Notch-type transmembrane protein. About 20 kb of dense Alu clustering was found just centromeric to the NOTCH3. (C) 1994 Academic Press, Inc.

15/7/17 (Item 3 from file: 434)
DIALOG(R)File 434:SCISEARCH(R)
(c) 1994 Inst for Sci Info. All rts. reserv.

12891144 Genuine Article#: BZ51X Number of References: 95
Title: FREQUENT MUTATIONS IN BREAST-CANCER
Author(s): CALLAHAN R; GALLAHAN D; SMITH G; CROPP C; MERLO G; DIELLA F; LISCIA D; LIDEREAU R
Corporate Source: NCI,BLDG 10,ROOM 5B50/BETHESDA//MD/20892; SAN GIOVANNI VECCHIO HOSP,USSL 1,PATHOL SECT/I-10123 TURIN//ITALY/; CTR RENE HUGUENIN/ST CLOUD//FRANCE/
Journal: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, 1993, V698, P21-30
ISSN: 0077-8923
Language: ENGLISH Document Type: ARTICLE

15/7/18 (Item 4 from file: 434)
DIALOG(R)File 434:SCISEARCH(R)
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12878833 Genuine Article#: MW455 Number of References: 111
Title: APICAL JUNCTIONS AND CELL SIGNALING IN EPITHELIA
Best Available Copy
Author(s): WOODS DF; BRYANT PJ
Corporate Source: UNIV CALIF IRVINE,CTR DEV BIOL/IRVINE//CA/92717
Journal: JOURNAL OF CELL SCIENCE, 1993, S17, P171-181
ISSN: 0021-9533
Language: ENGLISH Document Type: REVIEW
Abstract: Genetic analysis in Drosophila has led to the identification of several proteins that mediate cell-cell interactions controlling the fate and proliferation of epithelial cells. These proteins are localized or enriched in the adherens and septate junctions at the apical end of the lateral membranes between cells. The proteins localized or enriched at adherens junctions include Notch, which is important for the cell interactions controlling neuroblast and bristle patterning; Boss and sevenless, which are required for the cell interaction that establishes the R7 photoreceptor cell; and Armadillo, required for the wingless-dependent cell interactions that control segment polarity and imaginal disc patterning. Proteins localized at septate junctions include the product of the tumor suppressor gene dig, which is required for septate junction formation, apical basal cell polarity, and the cell interactions that control proliferation. The results suggest that the cell signalling events important for cell fate determination and for cell proliferation control in epithelia occur at the apical junctions. The migration of the nucleus to the apical surface of the epithelium for mitosis may enable it to interact directly with the junction-associated signalling mechanisms.

15/7/19 (Item 5 from file: 434)
DIALOG(R)File 434:SCISEARCH(R)
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12471887 Genuine Article#: LP726 Number of References: 53
Title: SPECIFIC TRUNCATIONS OF DROSOPHILA NOTCH DEFINE DOMINANT ACTIVATED AND DOMINANT-NEGATIVE FORMS OF THE RECEPTOR
Author(s): REBAY I; FEHON RG; ARTAVANISTSAKONAS S
Corporate Source: YALE UNIV,DEPT CELL BIOL,HOWARD HUGHES MED INST/NEW HAVEN//CT/06536; YALE UNIV,DEPT BIOL/NEW HAVEN//CT/06536
Journal: CELL, 1993, V74, N2 (JUL 30), P319-329
ISSN: 0092-8674
Language: ENGLISH Document Type: ARTICLE
Abstract: The Notch gene of Drosophila plays an important role in cell fate specification throughout development. To investigate the functions of specific structural domains of the Notch protein in vivo, a series of deletion mutants have been ectopically expressed under the hsp70 heat shock promoter. Two classes of dominant phenotypes are observed, one suggestive of Notch loss-of-function mutations and the other of Notch gain-of-function,mutations. Dominant activated phenotypes result from overexpression of a protein lacking most extracellular sequences, while dominant negative phenotypes result from overexpression of a protein lacking most intracellular sequences. These results support the notion that Notch functions as a receptor whose extracellular domain mediates ligand binding, resulting in the transmission of developmental signals by the cytoplasmic domain. Finally, the phenotypes observed suggest that the cdc10/ankyrin repeat region within the intracellular domain

plays an essential role in the postulated signal transduction events.

15/7/20 (Item 6 from file: 434)

DIALOG(R)File 434:SCISEARCH(R)
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11736855 Genuine Article#: JG755 Number of References: 74
Title: EXPRESSION PATTERN OF MOTCH, A MOUSE HOMOLOG OF DROSOPHILA-NOTCH, SUGGESTS AN IMPORTANT ROLE IN EARLY POSTIMPLANTATION MOUSE DEVELOPMENT
Author(s): DELAMO FF; SMITH DE; SWIATEK PJ; GENDRONMAGUIRE M; GREENSPAN RJ; MCMAHON AP; GRIDLEY T
Corporate Source: ROCHE INST MOLEC BIOL,ROCHE RES CTR,DEPT CELL &DEV BIOL/NUTLEY//NJ/07110; ROCHE INST MOLEC BIOL,ROCHE RES CTR,DEPT CELL &DEV BIOL/NUTLEY//NJ/07110; ROCHE INST MOLEC BIOL,ROCHE RES CTR,DEPT NEUROSCI/NUTLEY//NJ/07110
Journal: DEVELOPMENT, 1992, V115, N3 (JUL), P737&
Language: ENGLISH Document Type: ARTICLE
Abstract: The Notch gene of Drosophila encodes a large transmembrane protein involved in cell-cell interactions and cell fate decisions in the Drosophila embryo. To determine if a gene homologous to Drosophila Notch plays a role in early mouse development, we screened a mouse embryo cDNA library with probes from the Xenopus Notch homolog, Xotch. A partial cDNA clone encoding the mouse Notch homolog, which we have termed Motch, was used to analyze expression of the Motch gene. Motch transcripts were detected in a wide variety of adult tissues, which included derivatives of all three germ layers. Differentiation of P19 embryonal carcinoma cells into neuronal cell types resulted in increased expression of Motch RNA. In the postimplantation mouse embryo Motch transcripts were first detected in mesoderm at 7.5 days post coitum (dpc). By 8.5 dpc, transcript levels were highest in presomitic mesoderm, mesenchyme and endothelial cells, while much lower levels were detected in neuroepithelium. In contrast, at 9.5 dpc, neuroepithelium was a major site of Motch expression. Transcripts were also abundant in cell types derived from neural crest. These data suggest that the Motch gene plays multiple roles in patterning and differentiation of the early postimplantation mouse embryo.

15/7/21 (Item 7 from file: 434)
DIALOG(R)File 434:SCISEARCH(R)
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11694207 Genuine Article#: JD348 Number of References: 53
Title: DISORGANIZATION IS A COMPLETELY DOMINANT GAIN-OF-FUNCTION MOUSE MUTATION CAUSING SPORADIC DEVELOPMENTAL DEFECTS
Author(s): CROSBY JL; VARNUM DS; WASHBURN LL; NADEAU JH
Corporate Source: JACKSON LAB/BAR HARBOR//ME/04609; JACKSON LAB/BAR HARBOR//ME/04609; UNIV MAINE,DEPT BIOCHEM/ORONO//ME/04469
Journal: MECHANISMS OF DEVELOPMENT, 1992, V37, N3 (MAY), P121-126
Language: ENGLISH Document Type: ARTICLE
Abstract: Disorganization (Ds) is an exceptional mutation because of its diverse and profound developmental effects. Although other mouse mutations produce similar congenital defects, extreme pleiotropism, random occurrence, developmental independence of multiple defects, and type of anomaly make Ds unique. Examples of developmental defects include cranioschisis, rachischisis, thoracoschisis, exencephaly, hamartomas, and anomalies of appendages, digestive, genital and urinary tracts, sense organs, limbs and girdles, tail and pharynx. No other mutation in the mouse has such broad effects. Ds is therefore an

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important model for studying not only the genetic control of lineage determination and pattern formation but also the occurrence of sporadic congenital defects. To characterize the effects of gene dosage, we examined the viability and phenotype of Ds homozygotes and the phenotype of + / + / Ds trisomic fetuses. Occurrence of homozygotes was tested by intercrossing Ds / + heterozygotes, typing genetic markers that flank Ds, and examining homozygotes for morphological abnormalities. Not only were Ds homozygotes found in their expected frequency, homozygotes were not more severely affected than heterozygotes. Trisomies provide a direct test for determining whether Ds is a gain-of-function mutation. Trisomic fetuses were derived by crossing Ds / Ds homozygous mice to hybrid mice that were heterozygous for two related Robertsonian translocations. Two trisomic fetuses had developmental defects characteristic of DS mice. Together these results demonstrate that Ds is a completely dominant, gain-of-function mutation.

15/7/22 (Item 1 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00092498
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Gonadal Mixed Germ Cell Tumor Combined With a Large Hemangiomatous Lesion in a Patient With Turner's Syndrome and 45,X/46,X, +mar Karyotype (ARTICLE)

TANAKA, YUKICHI; SASAKI, YOSHIROH; TACHIBANA, KATSUHIKO; MAESAKA, HATAE; IMAIZUMI, KIYOSHI; NISHIHIRA, HIROKAZU; NISHI, TOSHIJI
Archives of Pathology and Laboratory Medicine
November, 1994; Brief Reports: pt_1135
LINE COUNT: 01428
0363-0153

In this report, we describe bilateral gonadal tumors with characteristic histopathological findings in a patient with Turner's syndrome who had 45,X/46,X, +mar mosaicism. The left gonad contained a gonadoblastoma and a remnant of streak gonad. The right gonad was entirely replaced by a 15X11X7-cm solid and cystic tumor, which was revealed to be a combination of a mixed germ cell tumor and a cavernous hemangiomatous lesion. The latter occupied approximately half of the entire tumor volume, and there was an incomplete boundarybetween it and the mixed germ cell tumor lesion. To our knowledge, this is the first reported case of Turner's syndrome with a combination of a mixed germ cell tumor and a hemangiomatous lesion inthe gonad. (Arch Pathol Lab Med. 1994;118:1135-1138)

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

15/7/23 (Item 2 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00086699
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Continuing Trends in the Prevalence of Right-Sided Lesions Among Colorectal Carcinomas (ARTICLE)

CADY, BLAKE; STONE, MICHAEL D.; WAYNE, JEFFREY
Archives of Surgery
May, 1993; Paper: p505
LINE COUNT: 00444
0004-0010

The shift of colorectal carcinoma location toward the proximal colon has been reported. This study documents that this statistically significant trend has continued through 1992. An increase in transverse and descending colon cancers is now apparent also. Only 59% of all large-bowel cancers occurred distal to the descending colon between 1978 and 1992. Both right-sided and distal large-bowel cancers have significantly decreased in size, yet the incidence and frequency of lymph node metastases have not changed over a 65-year interval (from 1928 to 1992). This constant proportion of lymph node metastases may suggest distinct biological subsets of cancers (lymph node avid vs lymph node avoidance). The progression from small size with fewer metastases to large size with more lymph node metastases occurs only in some of the smallest distal colorectal cancers.

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

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12/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1994 BIOSIS. All rts. reserv.

11066516 BIOSIS Number: 97266516
Ep-CAM: A human epithelial antigen is a homophilic cell-cell adhesion molecule
Litvinov S V; Velders M P; Bakker H A M; Fleuren G J; Warnaar S O
Dep. Pathol., State Univ. Leiden, Wassenaarsweg 62, P.O. Box 9603, 2300 RC Leiden, NET
Journal of Cell Biology 125 (2). 1994. 437-446.
Full Journal Title: Journal of Cell Biology
ISSN: 0021-9525
Language: ENGLISH
The epithelial glycoprotein 40 (EGP40, also known as GA733-2, ESA, KSA, and the 17-1A antigen), encoded by the GA-733-2 gene, is expressed on the baso-lateral cell surface in most human simple epithelia. The protein is also expressed in the vast majority of carcinomas and has attracted attention as a tumor marker. The function of the protein is unknown. We demonstrate here that EGP40 is an epithelium-specific intercellular adhesion molecule. The molecule mediates, in a Ca-2+-independent manner, a homophilic cell-cell adhesion of murine cells transfected with the complete EGP40 cDNA. Two murine cell lines were tested for the effects of EGP40 expression: fibroblastic L cells and dedifferentiated mammary carcinoma L153S cells. The expression of the EGP40 protein causes morphological changes in cultures of transfected cells-increasing intercellular adhesion of the transfectants-and has a clear effect on cell aggregating behavior in suspension aggregation assays. EGP40 directs sorting in mixed cell populations, in particular, causes segregation of the transfectants from the corresponding parental cells. EGP40 expression suppresses invasive colony growth of L cells in EHS-matrigel providing tight adhesions between cells in growing colonies. EGP40 can thus be considered a new member of the intercellular adhesion molecules. In its biological behavior EGP40 resembles to some extent the molecules of the immunoglobulin superfamily of cell adhesion molecules (CAMs), although no immunoglobulin-like repeats are present in the EGP40 molecule. Certain structural similarities in general organization of the molecule exist between EGP40 and the lin-12/Notch proteins. A possible role of this adhesion molecule in formation of architecture of epithelial tissues is discussed. To reflect the function of the molecule the name Ep-CAM for EGP40 seems appropriate.

12/7/4 (Item 2 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00087493
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Clinical Underestimation of Laryngeal Cancer Predictive Indicators (ARTICLE)

NAKAYAMA, MEIJIN
Archives of Otolaryngology

Sep, 1993; Original Article: p950
LINE COUNT: 00421
0003-9977

Objective: To evaluate the accuracy of clinical staging of advanced laryngeal cancer and to morphologically analyze the underestimated cases. Design: We conducted a retrospective histopathologic study of larynges from patients who had had total laryngectomy and were seen over a 21-year period. Setting: Academic tertiary referral medical center. Participants: Forty-one patients had clinically staged T3 laryngealcancer and 16 patients had T4 cancer. Intervention: Patients all underwent wide-field total laryngectomy.All larynges were processed as whole-organ serial sections in the coronal plane. Outcome Measure: The incidence of clinically underestimated laryngeal cancer. During this investigation, it became obvious that predictive indicators of thyroid cartilage involvement could be established.Results: Clinical underestimation had been made in approximately 50% of all T3 laryngeal cancer cases. The extent of thecartilage involvement in the underestimated group was characterized by microinvasion without penetration; approximately 90% of the cartilage involvement affected the thyroid notch and adjacent area. We established five objective indicators of thyroid cartilage involvement: (1) extensive cartilage ossification (risk for cartilageinvolvement, 73%); (2) glottic fixation (54%); (3) transglottic cancer (74%); (4) tumor length longer than the entire vocal fold length or longer than 2 cm (66%); and (5) extensive involvement of the anterior commissure (67%). Conclusions: Clinical underestimation of T4 laryngeal cancer was high because thyroid cartilage involvement was not accurately diagnosed. We believe our indicators of thyroid cartilage involvementwill provide objective guidelines for laryngeal cancer staging and will contribute to more reliable clinical cancer-staging decisions. (Arch Otolaryngol Head Neck Surg. 1993;119:950-957)

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

12/7/6 (Item 4 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00086703
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Determination of Tumor Aggressiveness in Colorectal Cancer by K-ras-2Analysis (ARTICLE)

FINKELSTEIN, SYDNEY D.; SAYEGH, RAOULF; BAKKER, ANKE; SWALSKY, PATRICIA
Archives of Surgery
May, 1993; Paper: p526
LINE COUNT: 00523
0004-0010

Markers that predict tumor aggressiveness on a case-by-case basis would enable individualization and optimization of oncologic therapy.To achieve this goal, the presence and specific type of K-ras-2 pointmutation was determined from formalin-fixed, paraffin-embedded tissuesites in 247 primary and 166 metastatic-recurrent colorectal adenocarcinomas, using a novel approach consisting of topographic tissue selection, DNA

amplification, and direct sequencing applicableto large and needle-biopsy-sized specimens. The results provide the basis for a genotypic classification of colorectal cancer capable of predicting individual tumor aggressiveness, including the pattern andextent of metastasis.

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

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15/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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11292950 BIOSIS Number: 97492950
An activated Notch suppresses neurogenesis and myogenesis but not gliogenesis in mammalian cells
Nye J S; Kopan R; Axel R
Dep. Neurol., Inst. Cancer Res., Coll. Physicans Surg., Columbia Univ., New York, NY 10032, USA
Development (Cambridge) 120 (9). 1994. 2421-2430.
Full Journal Title: Development (Cambridge)
ISSN: 0950-1991
Language: ENGLISH
P19 cells, a mouse embryonal carcinoma line, can be induced to differentiate into neurons. After induction, however, only a small subpopulation of cells develop as neurons, suggesting that equipotent cells adopt different cell fates. In invertebrate systems, the lin-12-Notch family of genes is thought to control the choice of cell fate. We have therefore asked whether activation of murine Notch (mNotch) regulates neuronal differentiation in P19 cells. We demonstrate that a dominant gain-of-function mutant of mNotch suppresses neurogenesis, as well as myogenesis in P19 cells. Overexpression of the full-length mNotch protein also suppresses neurogenesis. In contrast, the differentiation of glia is not affected by an activated mNotch homologue. These data indicate that mNotch may play a central role in the choice of cell fate in differentiating cells in culture and suggests that mNotch may play a similar role in the choice of fate in the developing mammalian embryo.

15/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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11066516 BIOSIS Number: 97266516
Ep-CAM: A human epithelial antigen is a homophilic cell-cell adhesion molecule
Litvinov S V; Velders M P; Bakker H A M; Fleuren G J; Warnaar S O
Dep. Pathol., State Univ. Leiden, Wassenaarsweg 62, P.O. Box 9603, 2300 RC Leiden, NET
Journal of Cell Biology 125 (2). 1994. 437-446.
Full Journal Title: Journal of Cell Biology
ISSN: 0021-9525
Language: ENGLISH
The epithelial glycoprotein 40 (EGP40, also known as GA733-2, ESA, KSA, and the 17-1A antigen), encoded by the GA-733-2 gene, is expressed on the baso-lateral cell surface in most human simple epithelia. The protein is also expressed in the vast majority of carcinomas and has attracted attention as a tumor marker. The function of the protein is unknown. We demonstrate here that EGP40 is an epithelium-specific intercellular adhesion molecule. The molecule mediates, in a Ca-2+-independent manner, a homophilic cell-cell adhesion of murine cells transfected with the complete EGP40 cDNA. Two murine cell lines were tested for the effects of EGP40 expression: fibroblastic L cells and dedifferentiated mammary carcinoma

L153S cells. The expression of the EGP40 protein causes morphological changes in cultures of transfected cells-increasing intercellular adhesion of the transfectants-and has a clear effect on cell aggregating behavior in suspension aggregation assays. EGP40 directs sorting in mixed cell populations, in particular, causes segregation of the transfectants from the corresponding parental cells. EGP40 expression suppresses invasive colony growth of L cells in EHS-matrigel providing tight adhesions between cells in growing colonies. EGP40 can thus be considered a new member of the intercellular adhesion molecules. In its biological behavior EGP40 resembles to some extent the molecules of the immunoglobulin superfamily of cell adhesion molecules (CAMs), although no immunoglobulin-like repeats are present in the EGP40 molecule. Certain structural similarities in general organization of the molecule exist between EGP40 and the lin-12/Notch proteins. A possible role of this adhesion molecule in formation of architecture of epithelial tissues is discussed. To reflect the function of the molecule the name Ep-CAM for EGP40 seems appropriate.

15/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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10830219 BIOSIS Number: 97030219

Analysis of phenotypic abnormalities and cell fate changes caused by dominant activated and dominant negative forms of the Notch receptor of Drosophila development

Rebay I; Fortini M E; Artavanis-Tsakonas S

Howard Hughes Med. Inst., Dep. Cell Biol., Yale Univ., New Haven, CT 06536-0812, USA

Comptes Rendus de l'Academie des Sciences Serie III Sciences de la Vie 316 (9). 1993. 1097-1123.

Full Journal Title: Comptes Rendus de l'Academie des Sciences Serie III Sciences de la Vie

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Language: FRENCH ENGLISH

The Notch gene of Drosophila plays an important role in cell fate specification throughout development. The Notch protein contains a large extracellular domain of 36 EGF-like repeats as well as 3 Notch/lin-12 repeats and an intracellular domain with 6 cdc10/ankyrin repeats, motifs which are highly conserved in several vertebrate Notch homologues (1-7). In this review we summarize the results of two recent studies which attempt to establish structurefunction relationships of the various domains of the Notch gene product (8, 9). The functions of various structural domains of the Notch protein in vivo were investigated using a series of deletion mutants which have been ectopically expressed either under the hsp70 heat-shock promoter or under the sevenless eye-specific promoter. Truncation of the extracellular domain of Drosophila Notch produces an activated receptor as judged by its ability to cause phenotypes matching those of gain-of-function alleles or duplications of the Notch locus (8). Equivalent truncations of vertebrate Notch-related proteins have been associated with malignant neoplasms and other developmental abnormalities (3, 6, 10, 11). In contrast, dominant negative phenotypes result from overexpression of a protein lacking most intracellular sequences. These results were extended by an analysis of activated Notch function at single-cell resolution in the Drosophila compound eye (9). It was shown that while overexpression of full-length Notch in defined cell types has no

4/7/1 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
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8646875 BIOSIS Number: 92111875
TAN-1 THE HUMAN HOMOLOG OF THE DROSOPHILA NOTCH GENE IS BROKEN BY CHROMOSOMAL TRANSLOCATIONS IN T LYMPHOBLASTIC NEOPLASMS
ELLISEN L W; BIRD J; WEST D C; SORENG A L; REYNOLDS T C; SMITH S D; SKLAR J
STANFORD UNIV. SCH. MED., STANFORD, CALIF. 94305.
CELL 66 (4). 1991. 649-662. CODEN: CELLB
Full Journal Title: Cell
Language: ENGLISH
Previously we described joining of DNA in the .beta. T cell receptor gene to DNA of an uncharacterized locus in a t(7;9)(q34;q34.3) chromosomal translocation from a case of human lymphoblastic leukemia (T-ALL). We now show that the locus on chromosome 9 contains a gene highly homologous to the Drosophila gene Notch. Transcripts of the human gene, for which we propose the name TAN-1, and its murine counterpart are present in many normal human fetal and adult mouse tissues, but are most abundant in lymphoid tissues. In t(7;9)(q34;q34.3) translocations from three cases of T-ALL, the breakpoints occur within 100 bp of an intron in TAN-1, resulting in truncation of TAN-1 transcripts. These observations suggest that TAN-1 may be important for normal lymphocyte function and that alteration of TAN-1 may play a role in the pathogenesis of some T cell neoplasms.

4/7/2 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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8583130 EMBASE No: 92259041
Sun-less tans may be possible with new synthetic hormone
Vanchieri C.F.
Journal Office, R. A. Bloch Intl. Cancer Info. Ctr., 9030 Old Georgetown Rd., Bethesda, MD 20814 USA
J. NATL. CANCER INST. (USA) , 1992, 84/16 (1234-1235) CODEN: JNCIA
ISSN: 0027-8874
LANGUAGES: English

4/7/3 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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08122975 92260975
Cancer, chromosomes, and genes.
Nowell PC
Department of Pathology and Laboratory Medicine, University of Pennsylvania, School of Medicine, Philadelphia.
Lab Invest (UNITED STATES) Apr 1992, 66 (4) p407-17, ISSN 0023-6837
Journal Code: KZ4
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW; REVIEW, ACADEMIC

(67 Refs.)

4/7/4 (Item 1 from file: 399)
DIALOG(R)File 399:CA Search(R)
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120130975 CA: 120(11)130975d DISSERTATION
TAN-1, the human homolog of Drosophila "Notch", is involved in chromosomal translocations in human lymphoblastic neoplasma
AUTHOR(S): Ellisen, Leif William
LOCATION: Stanford Univ., Stanford, CA, USA
DATE: 1992 PAGES: 80 pp. CODEN: DABBBA LANGUAGE: English CITATION: Diss. Abstr. Int. B 1993, 53(7), 3307 AVAIL: Univ. Microfilms Int., Order No. DA9234046
SECTION:
CA214001 Mammalian Pathological Biochemistry
CA203XXX Biochemical Genetics
IDENTIFIERS: gene TAN1 chromosome translocation lymphoblastic leukemia
DESCRIPTORS:
Leukemia,T-cell acute lymphocytic...
gene TAN-1 translocation in, in human
Recombination,genetic, translocation...
of gene TAN-1, in human T-cell acute lymphoblastic leukemia
Gene,animal...
TAN-1, chromosomal translocation of, in human T-cell lymphoblastic leukemia
Chromosome,human 7...
TAN-1 gene translocation from, in human T-cell lymphoblastic leukemia

4/7/5 (Item 1 from file: 442)
DIALOG(R)File 442:AMA Journals Online
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00050915

Secretory Carcinoma of the Breast (Article)

Rosen, Paul Peter, MD; Cranor, Milicent L.
Archives of Pathology & Laboratory Medicine
1991; 115: 141 (4)
0363-0153

Most studies of secretory carcinoma of the breast have been single case reports or separate analyses of the problem in either children or adults. We studied 10 female patients, aged 5 to 87 years. Most patients presented with a palpable mass, often near the areola. Five of six tumors were estrogen receptor negative; three analyzed for progesterone receptor were positive. Histologic patterns present in varying proportions were "classic" secretory carcinoma with microacini, abundant secretion with papillary features, and with prominent solid and papillary apocrine features. The tumors had strong reactivity for \alpha\-lactalbumin, S100, and carcinoembryonic antigen (polyclonal) and were negative for gross cystic disease full protein and anti-carcinoembryonic antigen (monoclonal). Six patients had mastectomy; four had local excision; none had axillary nodal

metastases intially. With follow-up of 3 to 72 months (mean, 47 months; median, 48 months), two patients treated by local excision had local recurrences, one patient had axillary nodal metastases. All patients are alive. Comparison of patients under and over 30 years of age revealed one important difference: younger patients had a longer interval between detection and biopsy -- 30 vs 2 months. Treatment recommendations are initial wide excision or quadrantectomy with low axillary dissection in most cases and, in premenarchal patients, strong effort to preserve the breast bud without jeopardizing local control.

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

4/7/6 (Item 2 from file: 442)
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00040379
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The Relationship of Basal Cell Carcinomas and Squamous Cell Carcinomas to Solar Keratoses (STUDIES )

MARKS, ROBIN; RENNIE, GEORGE; SELWOOD, THOMAS
Archives of Dermatology
July, 1988; 124: 1039-1042
LINE COUNT: 00202 WORD COUNT: 02797
ISSN: 0003-987X
CORPORATE SOURCE: Accepted for publication March 1, 1988. From the Anti-Cancer Council of Victoria, Carlton South (Dr Marks and Mr Rennie), and the Monash University Department of Social and Preventive Medicine, Alfred Hospital, Melbourne, Australia (Dr Selwood). Reprints not available. This work was partly supported by grants from the Peter Grant Hay Cancer Research Fund, the Skin and Cancer Foundation, Sydney, and the Anti-Cancer Council of Victoria. We thank Abe Dorevitch, Peter Foley, Greg Goodman, Danny Lanzer, Rosemary Nixon, Wendy Pakes, Michael Ponsford, and Ruth Salom who helped in these studies.

ABSTRACT: Six thousand four hundred sixteen people aged 40 years and over from three different locations in Victoria (Australia) were examined on the hands, forearms, head, and neck for the presence of solar keratoses and basal (BCCs) and squamous cell carcinomas (SCCs). Analysis of the relationship between these tumors revealed that the factors which predicted the likelihood of developing a solar keratosis were essentially the same as those that predicted the likelihood of developing a BCC and/or an SCC. These were age, sex, years of residence in Australia, indoor or outdoor occupation, tanning ability, propensity to sunburn, and location of residence. The presence of a coexisting solar keratosis was necessary for the development of an SCC in contrast to the development of a BCC. The findings suggest that unlike BCCs, the majority of SCCs in light-exposed areas may arise from preexisting solar keratoses. Whereas the prevalence of solar keratoses differed markedly in direct relation to the degree of insolation. This suggests that solar keratoses are a more sensitive indicator of sunlight exposure than invasive carcinoma.

* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *

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solar keratoses in Victoria. Med J Aust 1983; 2: 618-622.
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4/7/7 (Item 3 from file: 442)
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00037493
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Papillary Cystic Tumor of the Pancreas (LETTERS TO THE EDITOR )

WARREN, RENEE B.
Archives of Pathology and Laboratory Medicine
August, 1985; 109: 706-707
LINE COUNT: 00064 WORD COUNT: 00892
ISSN: 0363-0153
* * USE FORMAT 9 FOR FULL TEXT OF ARTICLE * *
CITED REFERENCES:

1. Morrison DM, Jewell LD, McCaughey WTE, et al: Papillary cystic tumor of the pancreas. Arch Pathol Lab Med 1984;108:723-727.

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4/7/8 (Item 1 from file: 444)
DIALOG(R)File 444:NEJM Online
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00112461
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Mechanisms of Disease: The Molecular Basis Of Leukemia (Review Articles)

Cline, Martin J.
The New England Journal of Medicine
Feb 3, 1994; 330 (5),pp 328-336
LINE COUNT: 00515 WORD COUNT: 07111
ISSN: 0028-4793
CORPORATE SOURCE: From the Division of Hematology, Center for the Health Sciences, 10833 LeConte Ave., Los Angeles, CA 90024-1678, where reprint requests should be addressed to Dr. Cline. - Supported by funds from the Ludwig Institute for Cancer Research, Middlesex Branch, London; the Leukaemia Research Fund, United Kingdom; and a Public Health Service grant (R01 CA 50275).

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